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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,265	08/19/2003	Jeffry G. Weers	0056.11	7484

21968 7590 10/07/2005

NEKTAR THERAPEUTICS
150 INDUSTRIAL ROAD
SAN CARLOS, CA 94070

EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 10/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/644,265	WEERS ET AL.	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-150* is/are pending in the application.

4a) Of the above claim(s) *8,30-132 and 139* is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-29,133-138, and 140-150* is/are rejected.

7)☒ Claim(s) *27 and 149* is/are objected to.

8)☒ Claim(s) *1-150* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08/19/2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/26/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-150 are pending.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-29 and 133-150, drawn to respiratory dispersions for the delivery of one or more bioactive agents, classified in class 424, subclasses 489 and 46.

II. Claims 30-49, drawn to a system for the pulmonary administration of bioactive agents comprising a fluid reservoir, a metering valve associated with said reservoir, and a stabilized dispersion in said fluid dispersion classified in class 96, subclass 116.

III. Claims 50-72, drawn to methods of forming stabilized dispersions comprising several steps, classified in class 424, subclass 46.

IV. Claims 73-93, drawn to methods for the pulmonary delivery of one or more bioactive agents comprising several steps, classified in class D24, subclass 110.

V. Claims 94-113, drawn to methods of making a functional metered dose inhaler comprising associating bioactive agents with perforated microstructures, dispersing said microstructures in a suspension medium comprising a propellant, and charging said metered dose inhaler with the resulting dispersion, classified in class D24, subclass 110.

VI. Claims 114-132, drawn to methods of stabilizing a dispersion comprising several steps, classified in class 424, subclass 45.

The inventions are distinct, each from the other because of the following reasons:

Inventions II and I are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the fluid reservoir of an aerosol device does not require a stabilized dispersion. In lieu of a stabilized dispersion the fluid reservoir could utilize a soluble composition. The subcombination has separate utility such as a medicament.

Inventions III/VI and I are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the products of Group I can be made from a different process, including an emulsion polymerization of a reaction mixture containing urethane monomers in a supercritical or liquid CO_2 medium, whereby particles isolated from said polymerization are exposed to acid to liberate CO_2 and dispersed in a mixture comprising an appropriate solvent and stabilizers/dispersing agents.

Inventions I and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP

§ 806.05(h)). In the instant case the process as claimed (Group IV) could be practiced using a stabilized dispersion of particles or powders that were not perforated.

Inventions V and I are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to methods of using a metered dose inhaler (Group V) and stabilized dispersions (Group I) comprising bioactive agents, propellant, a suspension medium, and dispersed perforated microstructures. Methods of using metered dose inhalers have a different mode of operation than stabilized dispersions. Whereas dispersions intended for therapeutic uses may be administered through the use of MDI's, they may also be administered in other routes, including orally and intravenously.

Inventions III/VI and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to methods of forming stabilized dispersions (Group III), methods for stabilizing dispersions (VI), and a device comprising (i) a fluid reservoir, (ii) a metering valve, and (iii) a stabilized dispersion. Methods of forming dispersions or stabilizing dispersions are not capable of being used with the devices of Group II, as this device plays no role in the formation or stabilization of dispersions. Furthermore, the inventions of Groups III and VI have different modes of operation than the devices of group II, because they require a sequence of steps in order to practice, whereas the invented products of II can exist and function independently of these methods.

Inventions II and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the process as claimed (Group IV) could be practiced using a dry powder inhaler in lieu of a device (i.e. system) for the pulmonary administration of a bioactive agent comprising a fluid reservoir, metering valve, and a stabilized dispersion.

Inventions II and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to methods (Group V) requiring the use of perforated microstructures having a mean aerodynamic diameter of less than about 5 μm, whereas the devices of Group II may be comprised of perforated microstructures having mean aerodynamic diameters larger than 5 μm.

Inventions IV/V/VI and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions are drawn to different methods altogether, including methods for the pulmonary delivery of one or more bioactive agents (Group IV) and methods for the pulmonary deposition using a metered dose inhaler (Group V); or are drawn to a related method comprising different steps (Group VI). As a result of these differences, these methods (Groups IV, V, and VI) would have different modes of operation than the methods of Group III.

Inventions V/VI and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions are drawn to different methods altogether, including methods for stabilizing dispersions by reducing attractive Van der Waals forces (Group VI); or are drawn to a related method comprising different steps (Group V). As a result of these differences, these methods (Groups IV, V, and VI) would have different modes of operation than the methods of Group III.

Inventions V and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to methods for increasing the pulmonary deposition of a biological agent using a metered dose inhaler (group V) and methods for stabilizing dispersions by reducing attractive Van der Waals forces (Group VI).

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

I n the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined

claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claims 7-12 are generic to a plurality of disclosed patentably distinct species comprising different kinds of surfactants. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

During a telephone conversation on September 9, 2005 with Mr. Ashok Janah, who was instructed by Michael Einschlag, one of the attorneys of record, to speak with the examiner regarding a restriction requirement and species election for the instant application a provisional election was made **without traverse to prosecute the invention of Group I, as defined by the**

examiner, and the species of claim 10 (i.e. a surfactant comprising a lipid). Affirmation of this election must be made by applicant in replying to this Office action. Claims 30-132 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 8 and 139 are withdrawn from consideration, because poloxamers do not correspond to the elected species of a lipid surfactant. Claims 7 and 138 have only been examined for surfactants encompassed by the elected species (i.e. phospholipids).

Drawings

The Examiner respectfully requests that Applicant resubmit Figs. 1-3, because the features mentioned in the "Brief Description..." are not readily apparent from the scanned images, such as the hollow characteristic of the particles depicted in Fig. 2. The scanned images of the photographs of Fig. 3 are unclear and for this reason one is not able to ascertain the claimed improved characteristics of the dispersions of the instant application relative to the stability characteristics of a commercial cromolyn sodium formulation.

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The use of the trademarks PLURONIC (p 24, line 5), SPAN 85 (page 23, line 28), ULTRA-TURRAX (pg 35, line 21), SPRAYMISER (pg 42, line 2), PROVENTIL (Table II), VENTOLIN (Table II), VANCERIL (Table V), AZMACORT (Table IV), and INTAL (Table IV), has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

The attempt to incorporate subject matter into this application by reference to McCutcheon's Emulsifiers and Detergents (see pg 24 of the specification) and to M. Sacchetti et al.'s "Inhalation Aerosols: Physical & Biological Basis for Therapy" (see pg 29 of the

specification) is ineffective because the incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, **or to a publication is improper**.

Claims 27 and 149 are objected to because of the following informalities: the word "anticholinergics" is misspelled as "antcholinergics. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-29 and 148 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "substantially" in claims 1 and 26 is a relative term, which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The word "substantially" is used to modify the meaning of the word "permeates." The term "substantially" suggests a degree of permeation of the suspension medium through the perforated microstructures, however the Applicant does not provide a metric by which to determine what degree of permeation constitutes "substantial permeation" of the perforated microstructure. A similar ambiguity exists in claim 26 as to the degree intended by the word "substantially" with regards to its use in the phrase "...substantially matches that of the suspension medium."

The remaining claims are rejected for depending upon a rejected claim.

Claims 21-23 and 148 recite the limitations "the mean geometric diameter (claims 21 and 148), the mean aerodynamic diameter (claims 22 and 23) " in first sentence of said claims. There is insufficient antecedent basis for these limitations in these claims. It is assumed that the limitations of claims 21-23 are in reference to the dispersed microstructures. If this assumption is correct, it is respectfully requested that Applicant clarify any ambiguity by appropriate modification of these claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 133-138, 141, 143 and 144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Platz et al. (WO 91/16038).

Applicant's claims are drawn to respiratory dispersions for the pulmonary delivery of one or more bioactive agents comprising a suspension medium comprising greater than about 20% w/w surfactant and at least one bioactive agent wherein said suspension medium comprises at least one propellant (claim 133); wherein said dispersed microparticles comprise greater than 30 % w/w surfactant (claim 134); wherein said propellant is a hydrofluoroalkane (claim 136); wherein said surfactant is selected from the group consisting of phospholipids and combinations thereof (claim 138); wherein said surfactant comprises a lipid (claim 141), wherein said lipid is a phospholipid (claim 143).

Platz teaches aerosol formulations of **biologically active solid polypeptide microparticles** (page 4, 1st two sentences at the start of the section entitled "Summary of the Invention").

Platz teaches that these aerosol formulations may be prepared as aerosol **suspensions** in a pressurized metered-dose inhaler (page 5, 1st sentence beginning on said page).

Platz teaches that to improve the dispersion in liquid suspension and to inhibit aggregation, some kind of **surfactant is preferably added** to the milled polypeptide powder. The surfactant includes **phospholipids, phosphatidylcholine, and natural lecithins** (page 7, 1st two sentences of the bottom paragraph of said page). The term phosphatidylcholine encompasses the terms dilauroylphosphatidylcholine, dioleylphosphatidylcholine, dipalmitoylphosphatidylcholine, disteroylphosphatidylcholine, dibehenoylphosphatidylcholine, and diarachidoylphosphatidylcholine.

Platz teaches that the polypeptide formulation for inhalation is dispersed by volatilization of a liquid propellant and the term **propellant** includes **hydrofluorocarbons (e.g. 1,1,1,2-tetrafluoroethane (HFC-134a))** (page 8, 2nd paragraph on said page).

Platz provides an example having specific amounts of a phospholipid surfactant (soy lecithin) ranging from 0.1 to 1.0% w/w (Example 3, Table 3). With regard to the limitations of claims 133 and 134 requiring 20% w/w and 30% w/w surfactant, respectively. The stated surfactant ranges are not considered critical, in the absence of unexpected results, because a person of ordinary skill in the art would have been expected to obtain compositions comprising similar amounts of surfactant upon the routine optimization of excipient ranges. The Applicant is required to demonstrate the criticality of the stated surfactant ranges.

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention that one could obtain the compositions of the instant application upon obvious and/or routine modification/optimization of the aerosol formulations taught by Platz et al. because Platz teaches suspended formulations comprising (1) biologically active polypeptides (i.e. bioactive agents); (2) lipid surfactants, including phospholipids such as phosphatidylcholine; and (3) propellants, including hydrofluorocarbons. Applicant's required minimum surfactant quantities are considered non-critical elements that a skilled artisan would have been able to obtain upon the routine optimization of excipient w/w ranges.

Thus, the claimed invention as a whole was *prima facie* obvious over the teachings of the prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7, 9-29, 133-138, and 140-150 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 and 9-29 and 72-87 of U.S. Patent No. 6,309,623. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are overlapping in scope.

Independent claim 1 of the instant application is drawn to a stable respiratory dispersion for the pulmonary delivery of one or more bioactive agents comprising a suspension medium having dispersed therein a plurality of perforated microstructures comprising at least one bioactive agent wherein said suspension medium comprises at least one propellant and substantially permeates said perforated microstructures.

Independent claim 1 of U.S. patent 6,309,623 is drawn to a stable respiratory dispersion for the pulmonary delivery of one or more bioactive agents comprising a suspension medium having dispersed therein a plurality of perforated microstructures having a mean aerodynamic diameter of less than 5 μm and comprising at least one bioactive agent wherein said suspension medium comprises at least one propellant and substantially permeates said perforated

microstructures wherein more than 30% of the average particle volume of the perforated microstructures is permeated by said suspension medium. ü

Although independent claim 1 of the instant application does not specify a percentage of the average particle volume of the perforated microstructures that is permeated by the suspension medium, the ambiguity of the term "substantially" renders it impossible to ascertain if this word results in the same claimed average particle volume permeation. Until the meaning of this term is clarified, it is considered to impart the limitation that more than 30% of the average particle volume of the perforated microstructures is permeated by said suspension medium.

Claim 1 of the instant application is silent as to the mean aerodynamic diameter of the perforated microstructures. However, because all the other critical elements are the same and the limitations of a mean aerodynamic and a mean geometric diameter of less than 5 μm are introduced by dependent claims 21-23, claim 1 is considered to have the same limitations and scope as claim 1 of U.S. patent '623.

Dependent claims 2-28 of both the instant application and U.S. patent 6,309,623 are verbatim, and therefore introduce the same limitations into the respective independent claims.

Dependent claim 29 of the instant application is drawn to stabilized dispersions comprising a suspension medium having dispersed therein a plurality of perforated microstructures comprising at least one bioactive agent wherein said suspension medium comprises at least one propellant and substantially permeates said perforated microstructures and wherein the bioactive agent is selected from a the group consisting of budesonide, fluticasone propionate, salmeterol, formoterol, and DNase.

Independent claim 29 of U. S. Patent No. 6,309,623 is drawn to stabilized dispersions comprising a suspension medium having dispersed therein a plurality of perforated microstructures having a mean aerodynamic diameter of less than 5 μm and comprising at least one bioactive agent wherein said suspension medium comprises at least one propellant and substantially permeates said perforated microstructures and wherein the bioactive agent is selected from a the group consisting of budesonide, fluticasone propionate, salmeterol, formoterol, gentamicin, LHRH, and DNase.

As discussed previously, it is considered that the perforated microstructures obviously have a mean aerodynamic diameter of less than 5 μm due to the limitations introduced by dependent claims 21-23 of the instant application. Claim 29 of U.S. patent '623 requires selection of the bioactive agent from a group consisting of two additional species not found in claim 29 of the instant application, specifically, gentamicin and LHRH. The additional two species in the group of bioactive agents found in claim 29 of U.S. patent '623 and absent in claim 29 of the instant application are obvious equivalent elements, because both gentamicin and LHRH are art recognized as bioactive agents known to be an antibiotic and a hormone, respectively. LHRH is Luteinizing Hormone-Releasing Hormone. Therefore claim 29 of the instant application contains all the components and limitations of claim 29 of U.S. patent '623.

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention that claim 29 of both the instant application and U.S. patent '623 have the same components or obvious modifications thereof, because the perforated microstructures of the instant application have the limitation of an average mean particle diameter of less than 5 μm, upon inclusion of the limitations of dependent claims 21-23 of the instant application, and the

inclusion or omission of art-recognized functionally equivalent components from a group (i.e. LHRH and gentamicin) is considered routine.

Independent claim 133 of the instant application is drawn to a respiratory dispersion for the pulmonary delivery of one or more bioactive agents comprising a suspension medium comprising greater than about 20% w/w surfactant and at least one bioactive agent wherein said suspension medium comprises at least one propellant.

Independent claim 72 of U.S. patent '623 is drawn to a respiratory dispersion for the pulmonary delivery of one or more bioactive agents comprising a suspension medium having dispersed therein a plurality of microparticles having a mean aerodynamic diameter of less than 5 μm and comprising greater than about 20% w/w surfactant and at least one bioactive agent wherein said suspension medium comprises at least one propellant.

Independent claim 133 of the instant application has the same components as claim 72 of U.S. patent '623, except it is silent regarding the microparticle mean aerodynamic diameter. Although the microparticle mean aerodynamic diameter is not explicitly stated it is considered to be an obvious characteristic of said microparticles upon consideration of the limitations introduced by dependent claims 146-148 of the instant application. It would have been obvious to a person of ordinary skill in the art at the time of the instant invention that claim 133 of the instant application and claim 72 of U.S. patent are of overlapping scope.

The remaining claims are rejected as being dependent upon a rejected claim.

Claims 1, 133-134, 136, 138, 143, 144, and 147-150 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 5-6, 8-11, 13, 14, and 16 of U.S. Patent No. 6,630,169. Although the conflicting claims are

not identical, they are not patentably distinct from each other because they are overlapping in scope.

Independent claim 133 of the instant application is drawn to a respiratory dispersion for the pulmonary delivery of one or more bioactive agents comprising a suspension medium having dispersed therein plurality of microparticles comprising greater than about 20% w/w surfactant and at least one bioactive agent wherein said suspension medium comprises at least one propellant.

Independent claim 1 of U.S. patent 6,630,169 is drawn to a **medicament** for the comprising a **plurality of microstructures** associated with one or more immunoactive agents, wherein said microstructures comprise **at least about 5% w/w of a biocompatible surfactant** selected from the group consisting of saturated and unsaturated lipids, nonionic detergents, nonionic block copolymers, ionic surfactants, cationic surfactants, biocompatible fluorinated surfactants, and combinations thereof. Medicaments are bioactive agents.

Although independent claim 1 of U.S. patent '169 lacks the propellant required by independent claim 133 of the instant application, this limitation is provided for by dependent claim 9. Claim 1 of U.S. patent '169 defines a lower limit for the quantity of surfactant as at least about 5% w/w, but no upper limit is stated. Because no upper surfactant limit is defined by claim 1 of '169, it is inclusive of the limitation of claim 133 of the instant application requiring greater than about 20% w/w surfactant. Therefore, independent claim 1 of U.S. patent '169 has the same critical components of independent claim 133 of the instant application, because medicaments are bioactive agents.

Independent claim 1 of the instant application is drawn to a composition comprising perforated microstructures, however, independent claim 1 of U.S. patent '169 does not require perforated microstructures. The limitation of perforated microstructures is provided by dependent claims 13 and 14 of U.S. patent '169.

The remaining dependent claims of the instant application and U.S. patent '169 and their respective limitations are discussed herein below. Claim 1 of U.S. patent '169 meets the limitation of claim 134, because no upper limit for the w/w quantity of surfactant is defined and the phrase "at least about 5% w/w surfactant" is inclusive of the phrase "greater than about 30% w/w surfactant." Claim 6 of U.S. patent '169 also meets the limitations of claim 134 of the instant application.

Claim 3 of U.S. patent '169 provides the limitation of a lipid that is a phospholipid (i.e. short-chain phospholipids).

Claim 5 of U.S. '169 provides the limitation for a phospholipid selected from the group consisting of dilauroylphosphatidylcholine, dioleylphosphatidylcholine, dipalmitoylphosphatidylcholine, disteroylphosphatidylcholine, dibehenoylphosphatidylcholine, diarachidoylphosphatidylcholine, and combinations thereof.

Claim 9 of U.S. patent '169 meets the limitations of claim 136 of the instant application requiring a hydrofluoroalkane propellant.

Claim 10 of U.S. patent '169 meets the limitations of claim 147 of the instant application requiring an aerodynamic diameter of said microstructures are between about 0.5 and about 5μm.

Claim 11 of U.S. patent '169 meets the limitations of claim 148 of the instant application requiring a mean geometric diameter of between about 1 and 5μm, because this range is encompassed by the range of claim 11 of U.S. patent of about between 0.5 and about 30 μm.

Claim 16 of U.S. patent '169 meets the limitations of claims 149-150 of the instant application requiring specific kinds of bioactive agents, including enzymes, proteins, peptides, combinations thereof, and DNase because the terms peptides, polypeptides, and proteins are either the same or in the case of enzymes and DNase are encompassed by said terms. Enzymes are proteins. DNase is an enzyme and therefore a protein.

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention that claims 1, 133-134, 136, 138, 143, 144, and 147-150 of the instant application and claims 3, 5-6, 8-11, 13, 14, and 16 of U.S. patent 6,630,169 have the same components, limitations, or are obvious modifications thereof, as discussed above.

Thus, the claimed invention as a whole was *prima facie* obvious over claims 3, 5-6, 8-11, 13, 14, and 16 of U.S. patent 6,630,169.

Conclusion

Claims 27 and 149 are objected to as described above. Claims 8 and 139 are withdrawn from consideration as being drawn to a non-elected species. Claims 30-132 are withdrawn from consideration as being drawn to a non-elected group per the above described restriction requirement. Claims 1-7, 9-29, and 133-150 are rejected.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni (Paddy) Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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James H. Alstrum-Acevedo, Ph. D.

Alton Pryor
Primary Examiner
A.U. 1616